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ORIGINAL ARTICLE

The Perinatal Outcomes of Asymptomatic Isolated Single Umbilical Artery in Full-term Neonates

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Background: Neonates with a single umbilical artery (SUA) are considered at increased risk for chromosomal and structural abnormalities, and an increased adverse perinatal outcome.
Objective: The specific aims of our study were to evaluate (1) the association of asymptomatic infants with isolated SUA and perinatal outcomes and (2) whether asymptomatic neonates with isolated SUA at birth need full investigation.
Methods: The inclusion criteria for the study were full-term neonates with isolated SUA delivered from January 1996 to December 2006. For a control group, we used the next consecutive two newborns delivered after the SUA case in the same maternity ward with matched gestational age and without phenotypic features suspicious for aneuploidy delivered after each SUA group subject. All prenatal, peripartum and delivery records were reviewed for maternal demographics, associated anomalies, karyotypic analysis, pregnancy complications and perinatal outcomes. All SUA cases had undergone sonogram for renal anomalies.
Results: We enrolled 14 and 28 cases into the SUA and control groups respectively. There was all normal karyotyping for the 14 cases. The placental weight in SUA was significantly lighter compared to that in the control group (597.1±175.4 *vs.* 709.3±95.2 g, $p=0.010$). All renal sonographic screens and karyotyping in the SUA group were normal. The incidence of small for gestational age (SGA) in SUA group was higher compared to control group (SGA, 5/14, 35.7% *vs.* 1/28, 3.6%, $p=0.011$) and less body length (48.7±5.0 *vs.* 50.8±1.8 cm, $p=0.028$).
Conclusion: SUA is a relatively rare finding. When a SUA is identified, the routine check of karyotyping and kidney sonography for possible chromosome and associated renal anomalies may be unnecessary. According to lighter placental weight probably causing the higher incidence of small for gestational age (SGA), pregnancies with isolated SUA should be carefully monitored for evidence of fetal growth restriction.

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1. Introduction

A two-vessel umbilical or single umbilical artery cord is the result of agenesis, either aplasia or atresia of one of the umbilical arteries. The prevalence of single umbilical artery (SUA) is about 1 in 100 live births; it is three to four times higher in multiple pregnancies. Neonates with an SUA are considered at increased risk of chromosomal and structural abnormalities, and increased adverse perinatal outcomes.[1] The presence of an SUA is recognized as a predictor for congenital anomalies, preterm delivery and low birth weight. It is therefore believable that if SUA is detected in a neonate, full investigatory work-up to detect occult malformations of various organ systems has to be performed. In some cases SUA can be an isolated feature. It is unclear if apparently asymptomatic infants with SUA need to be evaluated. A few autopsy-based studies show incidences of anomalies ranging from 25.0% to 81.8%, with a mean of 61.4%; however other studies based on screening of placentas or umbilical stumps of term neonates show anomalies ranging from 8.7% to 66.7%, with a mean of 27.0%. Observed anomalies most often involve the urogenital, gastrointestinal, cardiovascular, respiratory, and central nervous systems, as well as the face.[2] Similar anomalies have been noted on ultrasound among cases ascertained prenatally.[1,3] The number of umbilical vessels is identified as a routine examination in the delivery room. When an SUA is noted, intense exploration for other associated fetal anomalies should be undertaken. It is therefore conceivable that if SUA is detected in a neonate with obvious physical abnormalities, full work-up to detect occult malformations of various organ systems has to be undertaken. However, in some cases, SUA can be an isolated feature. It is unclear if apparently asymptomatic infants with SUA need the full investigation. The aims of our study were (1) to evaluate the association of asymptomatic infants with isolated SUA and perinatal outcomes and (2) to evaluate whether asymptomatic neonates with isolated SUA at birth need a full investigation such as radiography or sonogram.

2. Materials and Methods

The inclusion criteria for the study were full-term neonates with isolated SUA delivered at Shin-Kong WHS memorial Hospital from January 1996 to December 2006. This retrospective, case-controlled study was conducted to assess those infants with isolated SUA at birth. During the period of the study, there were 41,746 deliveries at the institution. The cases with SUA were identified by the International Classification of Disease 9 Codes (7475). All prenatal, peripartum and delivery records were reviewed for maternal demographics, associated anomalies, karyotypic analysis and pregnancy complications including maternal and paternal age, gravity, parity, delivery mode and conception route. Perinatal outcomes were defined as predictable parameters during delivery and included Apgar scores at 1 min and 5 min, gender, nuchal cord and placental weight. All SUA cases had undergone by renal sonography. Neonatal charts were also reviewed for gestational age, birth weight, small for gestational age, hospital stay by days and associated anomalies. Small for gestational age (SGA) was defined as having a birth weight less than the tenth percentile for gestational age, plotted on the Taiwan Intrauterine Growth Grid.[4]

For a control group, we used the next consecutive two newborns with matched age and without phenotypic features suspicious for aneuploidy delivered after each SUA group subject. These neonates all had a confirmed 3-vessel umbilical cord at birth. Gestational age was determined in relation to the estimated date of confinement, defined as 280 days from the last menstrual period.

Values are expressed as mean $\pm$ standard deviation (SD) unless indicated otherwise. Mann-Whitney U test was used for statistical analysis. The chi-square test was used to compare the categorical data. The statistical models fit the data remarkably well. The study was approved by the hospital's institutional review board. A p value of less than 0.05 was considered significant. Analyses were performed using the SPSS statistical package (SPSS Inc., Chicago, IL, USA).

3. Results

Forty-two infants were selected during the study period, 14 of which were SUA and the remaining 28 infants were in the control group. There was normal karyotyping in all 14 cases. Antenatal characteristics are presented in Table 1. Comparing the antenatal characteristics revealed no difference in maternal and paternal age, gravity, parity, delivery mode and conception route of assisted reproductive technology between the SUA and control groups. Comparing the neonatal outcomes revealed the incidence of small for gestational age (SGA) in the SUA group was higher compared to control group (SGA, 5/14, 35.7% *vs.* 1/28, 3.6%, $p=0.011$) and less body height (48.7 ± 5.0 *vs.* 50.8 ± 1.8 cm, $p=0.028$). The gestational age, birth weight (g), head girth (cm), chest circumference (cm) and duration of the hospital stay were similar in both groups. Table 2 shows that Apgar scores at 1 min and 5 min, gender and the frequency of the nuchal cord are similar. The placental weight

Table 1 Antenatal and neonatal demographics

	SUA (n=14)	Control (n=28)	p
Maternal age (yr)	30.7±3.9	29.5±4.2	0.405
Paternal age (yr)	34.6±5.7	32.0±5.4	0.089
Gravity	1.9±1.0	2.0±1.1	0.823
Parity	1.3±0.5	1.5±0.6	0.405
Cesarean delivery no. (%)	6 (42.9%)	4 (14.3%)	0.059
ART no. (%)	0 (0%)	2 (7.1%)	–
GA (wk)	38.7±2.6	38.6±1.3	0.436
BW (g)	2898.6±839.7	3110.2±333.3	0.228
SGA no. (%)	5 (35.7%)	1 (3.6%)	0.011*
HC (cm)	32.9±3.0	32.8±1.3	0.626
BL (cm)	48.7±5.0	50.8±1.8	0.028*
CC (cm)	31.2±3.9	31.7±1.4	0.947
Length of hospital stay (days)	4.9±1.9	4.2±1.6	0.150

*p<0.05. SUA = single umbilical artery; ART = assisted reproductive technology; GA = gestational age; BW = birth body weight; SGA = small for gestational age; HC = head circumstance; CC = chest circumstance.

Table 2 Perinatal demographics

	SUA (n=14)	Control (n=28)	p
Apgar score (1 min)	8.6±1.1	8.8±0.5	0.906
Apgar score (5 min)	8.9±0.3	9.0±0.2	0.864
Male, no. (%)	4 (28.6%)	16 (57.1%)	0.108
Nuchal cord, no. (%)	2 (14.3%)	5 (17.9%)	1.000
Placenta weight (g)	597.1±175.4	709.3±95.2	0.010*

*p<0.05. SUA = single umbilical artery.

in SUA was significantly lighter than that of the control group (597.1±175.4 *vs.* 709.3±95.2 g, p=0.010). All renal sonographic screenings and karyotyping in the SUA group were normal.

4. Discussion

The overall incidence of asymptomatic single umbilical artery, 0.03% observed in our study, is lower than previous reports (0.47%) that included symptomatic and asyptomatic SUA.[2,5] The symptomatic SUA is commonly associated with some relative anomalies and contributes to a poor outcome. SUA has been recognized as a soft marker for chromosomal abnormalities and congenital malformations.[6] Autopsy series from aborted and stillborn fetuses report a high incidence of associated malformations.[7] In our study, maternal age seemed to have no effect on the incidence of SUA cases. It is compatible with a previous study that showed advanced maternal age and associated chromosomal conditions were not major contributors to the incidence of SUA and related anomalies.[6] There was no significant relation between assisted reproductive technology (ART) and SUA. Due to the limitation of sample size, the association between ART and SUA was not conclusive. ART procedures such as in vitro fertilization and intracytoplasmic sperm injection are generally considered to be safe, but recent studies suggest a small excess of birth defects and low-birth weight in ART children. In our previous study, there were no significant congenital anomalies after the intervention of ART.[8] In the study by Bourke and colleagues,[9] infants with isolated SUA had a screening ultrasound scan. Those with abnormal scans underwent micturating cystourethrography and urine cultures. Vesicoureteric reflux (VUR) was documented in 4.5% of these infants.[9] There were no renal abnormalities in sonographic screening of all our SUA cases, which was not consistent with currently available evidence. It seems that the incidence of silent renal abnormalities in infants with isolated SUA is at least

threefold higher for severe malformations, and sixfold higher for any renal malformation compared to the general pediatric population.[9] We cannot demonstrate a higher incidence of renal structural anomalies by kidney sonography in our SUA group; the inadequate sampling size may play a role. In addition, voiding cystourethrogram (VCUG) and sonographic work-up for all possible occult congenital anomalies were not performed. Therefore, we cannot conclude that the SUA group had a similar incidence in all congenital anomalies excluding the kidney. We assumed that a screening renal ultrasound scan might be useful in detecting occult structural malformations of the urinary tract but wouldn't be routinely preserved in all neonates with SUA.

Four previous case reports of acute clinical manifestations of fetuses with a single umbilical artery include umbilical cord torsion, single umbilical artery stenosis associated with fetal death posttransfusion, spontaneous umbilical cord hematoma with associated fetal heart rate changes, and thrombotic occlusion of an umbilical vein varix causing fetal death.[10–13] The case report by Sherer et al[1] suggested that fetuses with SUA nuchal cords may be at increased risk of significant umbilical cord compression. We did not find any association between the complication of the nuchal cord and SUA. However, the affected cases of nuchal cord were limited in our study population, so the possibility of a type 2 error must be considered. The placental weight was significantly different statistically in the two groups. In our study, lower placental weight was shown in the SUA group. The SUA group also had a higher incidence of full-term neonates with small for gestational age. It is known that the umbilical artery is responsible for removing the metabolic waste from the fetus via the placenta.

Conclusions

In conclusion, SUA is a relatively uncommon finding. When an SUA is identified, a suggestion of a sonographic screen for associated renal anomalies wouldn't be routinely preserved in all neonates. Since lighter placental weight probably causes the higher incidence of SGA, pregnancies with isolated SUA should be carefully monitored for evidence of fetal growth restriction.

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